## REMARKS

### Status of the claims

Claims 6 and 10-19 are pending. Claims 1-5 and 7-9 have been cancelled. Claims 14-15 are withdrawn. Claims 6, 10 and 12-13 are amended herein. New claims 17-19 have been added. The amendments and new claims in no way add new matter and are fully supported by the specification. In particular, support may be found on page 15, line 4 through page 21, line 13, as well as figure 19, with regard to high molecular weight peptides. Support for the peptides of SEQ ID NOS: 14-17 can be found in Figures 22 and 23, as well as Example 12 of the specification.

### Sequence Listing

Enclosed herewith in full compliance with 37 C.F.R. §§1.821-1.825 is a Substitute Sequence Listing to be inserted into the specification as indicated above. The Substitute Sequence Listing in no way introduces new matter into the specification. Also submitted herewith in full compliance with 37 C.F.R. §§1.821-1.825 is an electronic CRF copy of the Substitute Sequence Listing. The electronic CRF copy of the Substitute Sequence Listing, file "2009-04-09-3749-0112PUS1_ST25.txt", is identical to the paper copy, except that it lacks formatting. In no way do the paper copy nor the electronic CRF copy of the Substitute Sequence Listing introduce new matter into the application.

The Sequence Listing is amended to add new SEQ ID NOS: 14-17, which are the amino acid sequences 815-852 (SEQ ID NO: 14), 815-853 (SEQ ID NO: 15), 815-854 (SEQ ID NO: 16), and 815-855 (SEQ ID NO: 17), of SEQ ID NO: 1. Thus, no new matter is introduced by these amendments.

### Rejection under 35 U.S.C. § 112, Second Paragraph

Claims 1-4, 6, 10-13 and 16 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as their invention. More specifically the Examiner asserts the following.

Claims 1-4 and 6 have been rejected as being vague and ambiguous because the claims reference potential cleavage cites of "Alcadein α", portions of the extracellular domains and enzymes that cleave Alcadein α. Claims 1-5 have been cancelled, thus rendering the rejection moot as to these claims. Claim 6 has been amended to be in independent form and limited to consist essentially of specific peptides. Withdrawal of the rejection is therefore respectfully requested.

Claims 12 and 13 have been rejected for lacking antecedent basis for the limitations "ratio" and "high-molecular-weight peptide". Additionally, claim 13 has been rejected as being vague for reciting terms such as "change" and cleavage sites for the peptide that are "closer." The Examiner states that the above terms are relative terms which are given without a point of reference within the claims. Furthermore, the Examiner asserts that claim 13 is missing a critical step, a step that identifies a therapeutic agent for Alzheimer's disease. Applicants traverse this rejection and withdrawal thereof is respectfully requested. Claims 12 and 13 have been amended to define the high-molecular-weight peptide comprising any one of SEQ ID NOS: 4 to 12 or 14 to 17 and one or more additional amino acids of SEQ ID NO: 1. The MPEP §2173.02 states,

> The examiner's focus during examination of claims for compliance with the requirement for definiteness of **35 U.S.C. 112**, second paragraph, is whether the claim meets the threshold requirements of clarity and precision, not whether more suitable language or modes of expression are available. When the examiner is satisfied that patentable subject matter is disclosed, and it is apparent to the examiner that the claims are directed to such patentable subject matter, he or she should allow claims which define the patentable subject matter with a reasonable degree of particularity and distinctness. Some latitude in the manner of expression and the aptness of terms should be permitted even though the claim language is not as precise as the examiner might desire. Examiners are encouraged to suggest claim language to applicants to improve the clarity or precision of the language used, but should not reject claims or insist on their own preferences if other modes of expression selected by applicants satisfy the statutory requirement.
>
> The essential inquiry pertaining to this requirement is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity. Definiteness of claim language must be analyzed, not in a vacuum, but in light of:
>
> (A) The content of the particular application disclosure;
>
> (B) The teachings of the prior art; and

> (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.
>
> In reviewing a claim for compliance with 35 U.S.C. **112**, second paragraph, the examiner must consider the claim as a whole to determine whether the claim apprises one of ordinary skill in the art of its scope and, therefore, serves the notice function required by 35 U.S.C. **112**, second paragraph, by providing clear warning to others as to what constitutes infringement of the patent. *MPEP 2173.02*

The present claims define the high-molecular-weight peptide as consisting of any one of SEQ ID NOS: 4 to 12 or 14 to 17 and one or more additional amino acids of SEQ ID NO: 1. As such, one skilled in the art would readily be able to determine whether an embodiment fell within the scope of the claims. The skilled artisan would merely need to determine whether the peptide in question contained any one of SEQ ID NOS: 1-17 and further contained any additional portion of SEQ ID NO:1. The specification on page 15, line 13 through page 21, line 13, Example 11, and figure 19, provides an in depth and thorough discussion on what is meant by high-molecular-weight peptide. As such, claims 12 and 13 are definite and clear as required under 35 U.S.C.§112, 2nd paragraph and withdrawal of the rejection is respectfully requested.

Claims 18 and 19 further define a high-molecular-weight peptide as being a cleavage product of SEQ ID NO:1, which has a higher molecular weight than the peptide of any one of SEQ ID NOS: 4 to 12 or 14 to 17. Support for claims 18 and 19 may also be found on page 15, line 13 - page 21, line 13. The metes and bounds of claims 18 and 19 would similarly be readily evident to one skilled in the art.

**Rejection Under 35 U.S.C §112, First Paragraph**

Claims 10-13 and 16 stand rejected under 35 U.S.C. §112, first paragraph as failing to comply with the enablement requirement. The Examiner suggests that the claims contain subject matter not described in the specification in such a way as to enable one skilled in the art to make or use the invention commensurate within the scope of the claims. In the previous office action issued July 7, 2009, upon which the Examiner relies in the present office action, the Examiner asserts that the invention is not enabled for diagnosis of Alzheimer's disease (AD) in samples other than those taken from the brain. With regard to claim 13, the Examiner asserts that there

is insufficient guidance was to how to determine the successful screening of potential therapeutic agents, i.e. no guidance as to why an agent that changes the amount of secreted Alcadein α fragment would be reasonably expected to be useful in treating AD. Applicants traverse these rejections and withdrawal thereof is respectfully requested.

Regarding the enablement of performing AD diagnostics with the instant invention, the Examiner's attention is directed to the specification (page 15, line 13- page 21, line 13, Example 11) and the figure 19. Especially from page 16, line 4, there is a description of the diagnostic steps; wherein it is stated, for example, "Therefore, Alzheimer's disease can be diagnosed by using the ratio of the amount of high-molecular-weight peptide to the total amount of the peptide of the present invention as an indicator, in addition to the determination of whether a certain amount of the peptide of the present invention in body fluid or the like." See also the steps as described in Example 11. In addition, the specification on page 53, line 19, spanning page 20 states,

> Namely, it was revealed that a qualitative change in β-Alc reflects a quantitative change in Aβ. A qualitative change in β-Alc (such as the increase in the ratio of long β-Alc) in cerebrospinal fluid or blood of patients reflects a qualitative change in Aβ. Therefore, the detection of β-Alc instead of the detection of Aβ42, which is highly aggregative, can find patients at an early stage or pre-patients of whom qualitative change is difficult to detect.

Thus, the specification describes the diagnosis of AB from samples of both cerebrospinal fluid and blood. The specification is therefore fully enabled for AB diagnosis using samples other than brain tissue and withdrawal of the rejection is respectfully requested.

With regard to claim 13 and new claim 19, screening methods for therapeutic agents for treating AD are fully described in the specification. See, for example, page 21, line 14 - page 23, line 20, Examples 9 and 12 and figures 20-23. Note in particular that page 23 of the specification states beginning at line 9,

> When a decrease in the secretion amount of the peptide caused by an agent to be screened is observed, the agent can be a candidate for a therapeutic agent for Alzheimer's disease When a change in the molecular species of the peptide, i.e., a change from a high-molecular-weight peptide to a low-molecular-weight peptide,

caused by an agent to be screened is observed, the agent also can be a candidate for a therapeutic agent for Alzheimer's disease."

Also, the detailed steps of screening for compounds are described in Examples 9 and 12 of the specification. Regarding how much the N-terminus or C-terminus the cleavage site is shifted to generate the high molecular weight peptide, the specification details from page 16, line 10 to page 17, line 9 how the shift occurs and illustrates examples of such shifts in figures 22 and 23 of Example 12. Thus, the specification fully enables one skilled in the art to screen for compounds having possible activity against AD and withdrawal of the rejection is respectfully requested.

In view of the above Amendment, Applicants believe the pending application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact MaryAnne Armstrong, PhD, Reg. No. 40,069, at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

Dated: APR 10 2009

Respectfully submitted,

By _____

MaryAnne Armstrong, PhD
Registration No.: 40,069
BIRCH, STEWART, KOLASCH & BIRCH, LLP
8110 Gatehouse Road
Suite 100 East
P.O. Box 747
Falls Church, Virginia 22040-0747
(703) 205-8000
Attorney for Applicant